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What's love got to do with it?
The potential role of oxytocin in the association between postpartum depression and mother-to-infant skin-to-skin contact

by

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Table of Contents

I. Abstract

Postpartum depression (PPD) is a maternal mental health problem associated with feelings of anxiety, stress, and depression. Skin-to-skin contact (SSC) is a health care intervention in which the infant is held prone against the mother's bare belly and chest. Oxytocin, the "hormone of love", is a neuropeptide that is both reduced in women with PPD and increased with SSC. This paper proposes that the physiological pathway of oxytocin during the postpartum period is the potential biological mechanism of the association between PPD and SSC. Further research is needed to examine this mechanism and support SSC as a successful intervention for the prevention and treatment of PPD.

II. Introduction

In 2011, there were 3,953,590 registered births in the United States.[1] Procreation is a major life event that has many associated health risks for both the mother and baby, lasting from pregnancy through childbirth and beyond. One maternal health risk that may develop following delivery is postpartum depression (PPD). PPD has an incidence rate of 1 in 8 postpartum women, affecting approximately 500,000 US births per year.[2] For the 9-16% of postpartum women per year in the United States who suffer from PPD, the incidence rate of PPD increases to 41% of postpartum women for subsequent pregnancies.[3]

This mental health problem can lead to a decreased ability to function in everyday life through feelings of anxiety, irritability, loss of pleasure or interest, withdrawal from social network, or thoughts of hurting oneself or others. These symptoms can arise as a result of physiological changes during the pregnancy itself, or due to the social stressors associated with caring for a new child. In addition to having a negative impact on the mother, PPD can also directly affect the children of mothers with PPD. These children may receive inadequate care, experience behavioral or developmental problems, or be at a higher risk for mental health problems later in life.[3,4] The high prevalence of this mental health problem and the associated negative impact for the health of the mothers and children make the topic of how to prevent and treat PPD of significant importance in the United States.

One potential intervention for the prevention and treatment of PPD is the practice of skin-to-skin contact (SSC). This technique involves holding the infant prone and in direct contact with the mother's belly and chest.[5] The skin-to-skin contact between the mother and infant, forming a singular unit known as a dyad, has been shown to provide health benefits to the infant through respiratory, cardiovascular, and thermoregulation with resultant glycemic regulation, as well as improved rates in breast feeding initiation and duration.[6-8] In addition to being a potentially life-saving intervention for the baby, SSC can also have a positive impact on maternal health through immediate postpartum dyad development. SSC is positively associated with improved bonding with the newborn and higher confidence in caring for the infant, factors which are negatively associated with the development of PPD.[9-12]

SSC was first introduced as an alternative to incubators for preterm infants in low-resource settings. Recently, SSC for preterm infants has been increasingly incorporated in Neonatal Intensive Care Units (NICUs) in the US. In 2002, a national study found 82% of respondents were currently practicing SSC in their NICUs.[13] However, the positive health outcomes of SSC are not limited to preterm infants. Full-term infants and their mothers can also benefit from SSC.[14-16] The integration of SSC in NICUs demonstrates the potential for bringing this intervention to scale for all new mothers throughout the country. This scalability is a necessary component to successfully introduce an intervention that would be capable of reaching the large percentage of women affected by PPD in the US.

Despite the high prevalence of PPD and the high rate of exposure to SSC in the NICUs in the US, the previous research on the potential association between PPD and SSC is extremely limited. The objective of this paper is to support the hypothesis that SSC is effective in preventing and treating PPD with a biological argument based on the hormonal shift of oxytocin which is common to both. The physiological pathway of oxytocin plays a role in the development of PPD, as well as in the maternal benefits attributed to SSC. Further research is proposed on the significance of oxytocin as the mechanism of the association between SSC and PPD.

III. Background

a. Postpartum depression

There are a variety of maternal mental health issues associated with the perinatal period. At the less severe end of the spectrum is postpartum blues, which describes a depressed mood that typically presents in the first week following birth and resolves within two weeks. Associated symptoms may include crying spells, anxiety, fatigue, insomnia, and decreased concentration. In the US, postpartum blues has an incidence of 50-70% of women in the early postpartum period.[17] Postpartum psychosis is at the other end of the spectrum, and is considered a psychiatric emergency. This condition is associated with mania, psychotic thoughts, and severe depression. Unlike the widely prevalent postpartum blues, postpartum psychosis presents in only 1 or 2 mothers out of every 1,000 births.[18]

Postpartum depression (PPD) lies between postpartum blues and postpartum psychosis on this spectrum of perinatal mental health problems. It can present with similar symptoms as postpartum blues, but with more severe depression, irritability, thoughts of self-harm, fear, guilt or withdrawal from others.[4] PPD symptoms can vary in intensity, from mild to severe, and duration, from weeks to months. In addition, the onset of symptoms can occur at any time within the first year following delivery, although the highest risk of incidence is within the first 3 months postpartum. This broad range of onset, symptoms, and duration results in a significant under-diagnosis of PPD and, therefore, a significant number of untreated cases.[3, 4]

When left untreated, PPD can result in negative outcomes for the mother and infant. Maternal health may suffer due to lack of sleep, poor nutrition, non-compliance with medical advice, or increased dependence on harmful substances.[3,4] The inability to perform daily activities due to decreased cognitive function can also trigger a cyclical effect when the infant's

needs are not met, causing feelings of guilt in the mother and resulting in increased depression. Children of mothers with PPD may have decreased cognitive skills, language development, and attention. These resulting deficiencies often present as behavioral problems and attachment difficulties that can result in life-long issues.[19]

The pathway to providing effective treatment for women with PPD begins with prevention and detection. Although the precise causes of PPD are yet to be determined, there are many factors associated with an increased risk of developing PPD. Major risk factors of PPD include increased stress brought about by a new child, a previous history of depression, low socioeconomic status, low social support, or low feelings of competence as a mother.[3] Screening for these risk factors of PPD can begin during pregnancy, distinguishing women who are more at risk and educating all women on symptoms and available options. Education about PPD prior to onset can diminish the shame and secrecy that is often associated with mental health conditions. Encouraging women to have an open dialogue with their physician and disclose symptoms of mental health problems will improve the detection of PPD. Once PPD is suspected, PPD can be confirmed through established assessment tools. Most commonly, health professionals rely upon the Edinburgh Postnatal Depression Scale for screening. This 10-item questionnaire is completed by the patient and is considered the most dependable PPD diagnostic tool with a sensitivity of 100% and a specificity of 95.5%.[20]

If detected, current treatment options for PPD include psychotherapy, pharmacotherapy, or a combination of both. Psychotherapy can be effective in easing stress triggered by the transition of relationships and the new roles associated with childbirth. This is

primarily provided through interpersonal therapy; however cognitive behavioral therapy can be beneficial when the mother's major PPD symptom is anxiety. Similarly to other major types of depression, pharmacotherapy treatment can be administered for PPD. Though, because PPD is experienced concurrently with the recommended breastfeeding time period, many concerns exist about the transfer of medication to the infant through breast milk. Previous studies have detected antidepressants transferred from the mother to the infant through breastfeeding; however the detected dose in the infant plasma was low enough to be considered tolerable and without sequelae. Often, the benefits of pharmacotherapy in the form of improved parenting are thought to outweigh any potential sequelae from the medication.[20] Regardless, many women and their physicians remain reluctant to rely on strong antidepressants in the postpartum period.

b. Skin-to-skin contact

Skin-to-skin contact between the mother and infant is a practice common to all mammals during the postpartum period to ensure that the newborn successfully transitions from an internal environment to an external one. After leaving the warmth and safety of the womb, the sudden exposure to cool air and new bacteria makes the newborn vulnerable to infection. Holding the infant in close proximity to the mother's heart, lungs, and skin allows the mother to continue to provide heat and safety after birth. SSC teaches infants to function independently outside of the womb by synchronizing their own physiology with the heartbeat,

breathing, temperature, and healthy bacteria of their mother.[21] Continuous SSC was first introduced as an alternative to using incubators in areas with high neonatal infection and mortality rates and limited resources.[5] Although it is a biologically natural process, the practice of SSC is considered an intervention because it differs from the current conventional childbirth routine during which the infant is immediately isolated in order to be cleaned and assessed. This isolation continues as infants are placed in car seats and other transport devices, not receiving direct contact with the parent. In SSC, the infant is held in an upright prone position against the bare chest of the parent, with both the parent and infant covered as a single unit, or dyad, by clothing or a blanket.[5] As the focus of this paper is on the association of SSC with maternal PPD, the parent of this dyad is assumed to be the mother. Besides infant cardiorespiratory stability and thermoregulation, the act of holding the infant in this position also promotes frequent and exclusive breastfeeding, improved mother-infant bonding and maternal satisfaction, and an increased and more mature sleep for the infant. These health benefits result in the association of SSC with an overall reduction in mortality, illness, infection, and length of stay in the hospital for both preterm and full-term infants.[8-12]

The terminology surrounding the practice of SSC varies throughout the literature. Related terminology includes Kangaroo Care, Kangaroo Mother Care, and babywearing. Historically, Kangaroo Care (KC) describes the practice of SSC as a substitute for incubator care. In recent literature, SSC and KC are often used interchangeably, requiring each individual study to differentiate the protocol-specific requirements of the intervention. Kangaroo Mother Care (KMC), on the other hand, is the terminology used by the World Health Organization (WHO) to

identify the practice of SSC in combination with exclusive breastfeeding. The WHO's intention of this pairing is to distinguish the critical role of the mother in caring for the newborn.[7] In contrast to the more clinical use of SSC, KC, and KMC, babywearing indicates the practice of wearing or carrying a baby in a sling or carrier while both the infant and mother are clothed.[22] Based on this definition, babywearing does not offer direct contact between the mother and child or specify the positioning of the infant, and so it is not considered to provide all of the health benefits associated with SSC. Instead, this practice is primarily used as a form of transport, not as a healthcare intervention.[22]

IV. Oxytocin

Oxytocin is a nine amino acid neuropeptide referred to colloquially as the "hormone of love". Oxytocin is involved in physiological reactions to a variety of situations associated with feelings of love, ranging from orgasms to childbirth. This hormone is primarily synthesized in the hypothalamus and secreted by the posterior pituitary, although it can also be generated in areas such as the uterus, placenta, and heart. The oxytocin receptor is a transmembrane receptor that functions to activate numerous intracellular pathways. One major pathway initiated by the binding of oxytocin to the oxytocin receptor results in the stimulation of muscle contraction. In fact, the most well-known function of oxytocin is to stimulate the contraction of the uterus in childbirth and the milk ducts during breastfeeding.[23-25]

The perinatal effects of this hormone begin with a spike in oxytocin levels during labor. In terms of gross anatomy, this sudden increase correlates to the contractions of the uterus

with subsequent descent of the baby through the birth canal. At the cellular level, oxytocin binds to its receptor, initiating the signal pathway to generate myometrial muscle contractions. This hormonal pathway continues until the placenta is delivered, at which time the levels of oxytocin begin to decrease.[25-27] When the mother breastfeeds, oxytocin functions to stimulate milk let-down by initiating the signal pathway to contract mammary myoepithelial cells. Oxytocin continues to be released as the infant suckles to further stimulate milk ejection.[28]

In addition to physical responses, oxytocin can also elicit a psychological response. Oxytocin and oxytocin receptors within the brain correspond to numerous behavioral characteristics. For instance, oxytocin is positively associated with social bonding, maternal inclination, maternal affectivity, and stress-responsiveness.[29] Increased concentrations of oxytocin can lead to a reduction in pain for both the mother and infant. Oxytocin is also capable of regulating cortisol levels to generate or enhance feelings of love and attachment.[30]

V. Hormonal shift during postpartum depression

During pregnancy, plasma hormones such as estrogen, progesterone, prolactin, aldosterone, cortisol, and oxytocin gradually increase until birth. The combined effect of the influx of these hormones elicits many physiological changes needed for birth. However, following birth, the concentration of many of these hormones drastically drops.

This dramatic shift is necessary for the onset of lactation, but is also thought to contribute to the development of PPD. However, the exact hormonal attribution remains

unclear. Prior research has been inconsistent in showing whether the steroid hormones estradiol and progesterone determine causation of PPD. Studies on the role of stress hormones, such as cortisol, in the development of PPD are also inconclusive. Even though the levels of stress and steroid hormones experience a significant shift during the immediate postpartum period, none appear to independently cause PPD.[31-34]

In regard to the hormone oxytocin, however, the association with PPD has been widely unstudied until recently. Recent reports indicate that people with lower levels of plasma oxytocin are found to be more likely to exhibit symptoms of depression.[35] Unlike women with PPD who have difficulties showing affection for their children, women with high levels of plasma oxytocin exhibit more affection when interacting with their children.[36, 37] While the precise mechanism through which this occurs is not yet identified, it is believed that the effects of oxytocin on postpartum behavior cause women to better manage the physiological and social changes of childbirth that often lead to PPD. Current literature suggests that with further study, there is the potential for oxytocin to be manufactured as a pharmacological treatment for PPD due to its ability to regulate depression, anxiety, and maternal behavior.[38]

VI. **Hormonal shift during skin-to-skin contact**

When the infant is placed in SSC with the mother, a surge of oxytocin and other hormones are released in both the mother and baby.[39] The maternal affectionate contact achieved through SSC is positively associated with maternal oxytocin levels. Similarly, the

mother's close proximity to the infant required by SSC is also positively associated with maternal oxytocin levels. [40-42]

In addition, SSC can lead to increased levels of oxytocin by way of improved breastfeeding practices. SSC contributes to more positive breastfeeding experiences, starting with the first latch. With increased frequency, duration, and longevity of breastfeeding, the increase in infant suckling causes an increase in oxytocin stimulation.

VII. Previous research on the association between SSC and PPD

Knowing this, it can be reasoned that SSC is a potential preventative or therapeutic intervention for PPD. However, the current research on this association is extremely limited. The three available studies are small in subject accrual, have varying inclusion criteria, and differ in methods of defining SSC and detecting PPD. However, despite the limitations of these studies, all three support the theory that SSC can decrease the incidence and prevalence of PPD.

In Brazil, de Alencar et al. conducted a study on treating PPD with SSC from December 2006 to July 2007.[43] The study included 180 mother-infant dyads, with infants from singleton births, weighing less than 2000g at birth and without malformations. Mothers were all low-income; however those who were illiterate and/or had a previous history of depression were excluded. SSC was initiated upon discharge from the NICU and performed as often and as long as possible, with a minimum of 1-2 hours at a time. SSC was continued until the infant reached

a minimum level of health, determined by a weight gain of 10-15g per kg per day for three consecutive days, feeding well, maintaining temperature, and confidence of mother in caring for the infant. PPD among the study subjects was assessed using the Postpartum Depression Screening Scale at time of admission to the NICU and at completion of SSC study period. This study found a statistically significant ($p<0.001$) decrease of PPD among mothers in the study from an initial prevalence of 37.3% to 16.9% following SSC, with no new cases of PPD.[43]

The strengths of the de Alencar et al. study include its larger study population and its clear definition of SSC practice requirements. The limitations of this study include a higher than usual prevalence of PPD (37.3% compared to an international estimate of 13%), a non-definitive diagnosis of PPD, and a limited follow-up period.[43] The study would be strengthened if conducted with a representative sample assessed by the Edinburgh Postpartum Depression Scale over the first year following birth. In addition, the lack of a control group does not allow for the establishment of causation in SSC diminishing PPD among study subjects because all subjects received the same treatment. A comparison group of low-income women with singleton births who did not participate in SSC would have been beneficial in identifying the importance of SSC in the decrease of PPD among the intervention population. Another important component that was omitted from this study was the impact of infant feeding practices. As breastfeeding is independently associated with decreased PPD, it is necessary to identify if this pathway influences the effect of SSC on PPD.

The study on SSC and PPD in South Korea by Ahn et al., on the other hand, controlled for breastfeeding status as a possible confounder.[44] This 2006 study followed 20 mother-infant

dyads, 10 practicing SSC and 10 controls, over a period of 3 weeks. Eligibility was determined on birth at <36 weeks gestation, a birth weight of <1800g, and a physiologically stable infant. The two groups were matched in breastfeeding or formula feeding practices and only differed by the intervention group spending a minimum of 10 total hours in SSC over the 3 week study period. PPD was determined using the Edinburgh Postnatal Depression Scale and maternal attachment was assessed using an adapted Muller questionnaire. All mothers showed moderate levels of depression at study initiation, yet both groups showed no signs of depression following the study. The results of this study did not distinguish a decrease in depression unique to the SSC group, however the SSC group did report higher attachment scores than the control group ($p=0.003$).[44]

The strengths of the Ahn et al. study include the case-control study design and the controlling for confounding by breastfeeding status. The ten intervention mother-infant dyads were matched by gestational age and birth weight with 10 pairs who formed a control group. The intervention and control groups had comparable general characteristics, breastfeeding and formula feeding practices, and overall healthcare treatment (apart from SSC). However, the study population is extremely small and from a single NICU, making the generalizability of the results difficult. In addition, the minimal requirement of 10 hours of SSC over a period of 3 weeks by the intervention group is a very low threshold and might limit the degree of impact of the intervention on the outcome.[44]

To further assess the distinction between the impact of SSC and breastfeeding practices on decreasing PPD, Abul-Fadl conducted a study in Egypt among 90 mother-infant dyads.[45] All

90 infants were low birth weight, with 30 treated with SSC and exclusively breastfed, 30 treated with incubators and exclusively breastfed, and 30 treated with incubators and artificially fed. PPD among study mothers was determined using the Beck Depression Inventory, and the change in PPD from study initiation to 6 weeks postpartum was compared across the three study groups. The results of this study show that SSC paired with exclusive breastfeeding led to a statistically significant decrease in PPD compared to mothers of either group receiving incubator care, regardless of breastfeeding practices.[45]

The main strength of this study is the three arm study design to compare the effects of SSC and breastfeeding with PPD. An additional strength of this study is the discovery of possible limitations present when studying SSC in the NICU setting. The supplemental assessment of knowledge, attitudes, and practice of SSC among NICU staff found a reluctance toward implementing SSC in the hospitals. This finding revealed a possible barrier to proper SSC implementation in NICUs. If health care providers are reluctant to teach and support SSC, mothers might be less compliant or less frequent with SSC. The resulting lower quantity and quality of SSC has the potential to impact the overall findings of its effect on PPD.[45]

Overall, the previous studies have the similar methodological limitation of studying only mothers with premature or low birth weight infants. The study subjects were all chosen based on admission to a NICU, however the infants were in stable conditions throughout the study period. This narrow subject selection eliminates the subset of women who develop PPD following stillbirths or neonatal deaths, those with severely ill infants, and those with infants born in good health. In addition, the assessment of the duration and frequency of SSC is

inconsistent throughout the literature, as is the determination of PPD diagnoses. SSC had minimal requirements of 1 to 2 hours at a time, a total of 10 hours over 3 weeks, or any amount over 6 weeks. PPD was determined using the Postpartum Depression Screening Scale, the Edinburgh Postpartum Depression Scale, and the Beck Depression Inventory. These inconsistencies weaken the research by making it difficult to substantiate the findings of all three studies.

There is still much to be learned about the association between SSC and PPD. In particular, the mechanism in which this association might occur has yet to be determined. Potential pathways, such as the role of maternal oxytocin, have previously been examined in association with either PPD or SSC, but not both.

VIII. Proposed Research

Further research is needed to support the association of PPD and SSC and determine if oxytocin is the biological mechanism responsible for mediating this pathway. The most effective way to accomplish this is through a large-scale, long term randomized control trial. This study would be conducted in health care facilities throughout the United States with a more inclusive subject population of mother-infant dyads to better represent the health of the general population (in both infant health and maternal PPD). To accomplish this, the subject population would be randomized into SSC intervention and comparison groups prior to birth. Although this would limit the study population to women who attend antenatal care visits, this

would allow SSC to begin immediately after birth and the consent process would not burden the women during labor. This early recruitment would enable the study the primary objective of preventing PPD, with the secondary objective of treating PPD.

When randomized, women would be assigned to either the SSC intervention arm or to the control arm. Women on the intervention arm would receive instructions on the technique of SSC by their healthcare provider. Following birth, these women would complete a recommended minimum of one hour of SSC every day (with a minimum of 30 minutes per session) for the first 3 months postpartum. This coincides with the time during which the onset of PPD is the highest. After the first three months, the women would continue a minimum of 5 hours every week for the remainder of the year. These minimum time requirements for SSC are chosen to enable the participation of women who might have to return to work shortly after childbirth. In this way, subject selection would not be limited to people with higher socioeconomic status who are able to spend more time with the infant. Additional future studies could examine if there is a minimum threshold of time spent in SSC that would still provide health benefits. This data would be important in the development of maternity leave policies in support of flexible work schedules, extended paid leave, or bringing infants to the workplace.

As this study design would require women to be followed for the first year postpartum, it is recommended that these visits coincide with the recommended well-baby visits at months 1, 2, 4, 6, 9, and 12.[46] During these visits, as well as during the initial screening visit, women would be assessed through patient-completed questionnaires and the collection of biological

specimens. The questionnaires would include the standardized Edinburgh Postnatal Depression Scale for the detection of PPD, as well as queries on infant feeding practices, SSC practices (if on the intervention arm), health of the infant, and health of the mother. The blood specimen collected would be assessed for oxytocin levels. These variables, along with demographic information, maternal history of depression, and gestational age, would provide the information needed to identify the potential association between SSC and PPD and whether oxytocin facilitates that association.

For women with questionnaire responses indicative of PPD, further follow up would be conducted by their health care provider to ensure a definitive diagnosis. All women who develop PPD, regardless of SSC randomization, would continue to receive the standard of care in addition to their study participation. Therefore, the women on the SSC arm with PPD would receive SSC as a supplemental therapy. This would be done for ethical purposes, so that no one is withheld treatment during the study.

This study design would require a large sample size in order to accrue enough women with PPD to have substantial power when analyzing the potential effect of SSC. The measured outcomes would compare the incidence rates of PPD between the intervention and control arms, as well as any potential differences in the duration or severity of PPD for all women who develop PPD. If this intervention caused even a 10% reduction in the incidence of PPD, it would equate to 50,000 fewer PPD effected births per year in the US. With prevention as the primary objective, there is the possibility that the number of women who develop PPD on the

intervention arm would be low. If that is the case, an additional study would be designed to independently assess the therapeutic potential of SSC for women already diagnosed with PPD.

IX. Conclusion

PPD affects a large percentage of women and families in the US, and SSC is a low-cost and simple practice that has the possibility of diminishing its negative outcomes. The possible biological reason for this effect is due to the role of oxytocin in the mother during the postpartum period. This hormonal pathway suggests that the practice of SSC can prevent or treat the symptoms of PPD, such as anxiety and lack of confidence in caring for the infant, by moderating the maternal levels of oxytocin. Higher concentrations of oxytocin are produced through increased maternal contact and proximity with the infant, binding to the oxytocin receptors in the regions of the brain responsible for developing healthy maternal affection.

Ideally, a large-scale and longer term randomized control trial should be conducted to produce valid and generalizable results. Conducting further research with a large enough representative sample to adjust for the health of the infant and investigate the biological mechanism is both feasible and able to generate highly beneficial data. The identification of the biological pathway and the conduction of improved research studies are important factors in further establishing a comprehensive understanding of how these factors interact. With this information, SSC might begin to be utilized in the postpartum period to decrease the prevalence of PPD and enhance the lives of mothers and infants around the world.

X. References

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